

## REMARKS

### **I. Introduction**

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and these comments.

### **II. Status of the Claims and Summary of Amendments Thereto**

Applicants previously cancelled claims 2, 4, 5, 13, and 18-22. Presently, Applicants request cancellation of claims 1, 15, 16 and 25 without prejudice or disclaimer. Applicants reserve the right to pursue cancelled subject matter in this or another application.

Claim 14 is amended to incorporate more conventional language for a method of treatment, and to recite specific cancers for which there is unambiguous and enabling description, as Applicants discuss below. Support for the amendment can be found in the specification at paragraphs 0029, 0030, 0268 (Table 1), and 0271 (Table 2).

Claim 23 is revised to replace the compound designated as 65G with a cleaner depiction, unobscured by “65G.”

The preamble of amended claim 24 identifies more clearly the subject matter as a method for producing one of several macrolactones, not just Peloruside A. Further changes to the claim add punctuation that is appropriate for Markush groups. The amendments prompted the cancellation of claim 25 and clarifying amendments to dependent claim 26.

Finally, claim 28 is recast as independent, to incorporate the subject matter of cancelled claim 1.

After entry of the foregoing amendments, claims 3, 6-12, 14-17, and 23, 24, and 26-28 will be pending. The amendments do not introduce any new matter, nor do they necessitate an additional search burden on the Examiner. Additionally, the amendments eliminate or at least reduce the number of stated concerns, placing the application into better condition for appeal. Therefore, Applicants respectfully urge the PTO to enter the amendments.

### III. The Office Action

Applicants gratefully acknowledge the PTO's allowance of claims 3, 6-12, 17, and 28. *See* Office Action summary and page 6. At issue now are concerns that should be mooted by the foregoing amendments.

#### A. Rejection of Claims Under 35 U.S.C. § 102(b)

The PTO maintained its rejection of claims 1 and 23 for alleged anticipation by the Northcote and West publications of record. Office Action at 2. Additionally, the PTO stated without explanation that the cited prior art also teaches the methods of claims 14-17 and 28.<sup>1</sup> In primary support of the rejection, the PTO discounted the de Brabander declaration, instead considering that each cited publication teaches the isolation of peluroside A from a marine sponge such that a skilled artisan could determine the structure of peluroside A. *Id.*

While Applicants do not acquiesce to the PTO's reasoning or conclusion, cancellation of claim 1, 15, and 16 moots the rejection. To the extent that the rejection also might apply to the remaining claims, Applicants respectfully traverse the rejection.

The inclusion of claim 23 in this ground for rejection is in error. Inasmuch as either cited publication teaches any compound, it is only peloruside A, which claim 23 does not encompass. Therefore, the cited publications do not anticipate claim 23.

Northcote and West also fail to support the rejection as to present method claim 14, which does not recite peloruside A. Thus, the cited prior art fails to anticipate.

Finally, neither Northcote nor West anticipates allowed claim 28. While it is not clear that the PTO intended to reject this claim,<sup>2</sup> it is clear that neither publication hints at the accumulation from a marine sponge of any appreciable amount of peloruside A, much less the "therapeutically effective" amount prescribed by the claim. At the very least, Northcote or West fail to anticipate for want of an enabling prior-art disclosure or suggestion of the required amount of peloruside A to practice the claimed method.

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<sup>1</sup> The PTO twice stated that claim 28 is allowed. Accordingly, Applicants request the PTO to clarify its reason for including claim 28 under this rejection.

<sup>2</sup> *Id.*

For these reasons, the claims are novel over Northcote and West. Accordingly, the rejection cannot be sustained, and Applicants respectfully request its withdrawal, therefore.

**B. Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph**

The PTO rejected claims 23 and 24 for alleged indefiniteness. Office Action at 3. In particular, the PTO requested correction to an obscured formula 65G in claim 23, and punctuation in the Markush group of claim 24. Applicants kindly thank the PTO for calling these informalities to their attention. The claim amendments overcome the stated grounds for rejection, which should be withdrawn.

**C. Objection to the Claims**

The PTO objected to claims 25-27, alleging duplication vis-à-vis claim 24, which the PTO considered to “cover the same thing” as dependent claims 25-27. Office Action at 3.

The claims as amended do not “cover the same thing.” Thus, the preamble of claim 24 indicates that the subject process produces one of several macrolactones. The clarification is consistent with recited final step (i), which specifies the macrolactones. Claim 25 is cancelled, while claim 26 requires that the macrolactone produced is peloruside A. Finally, claim 27 recites an *enantiomer* of peloruside A. None of the claims, therefore, “cover[s] the same thing.” Applicants therefore request the PTO to withdraw this objection.

**D. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph**

The PTO rejected claim 14-16 under 35 U.S.C. § 112, first paragraph for alleged want of enablement. Office Action at 4. In support of the rejection, the PTO devoted commentary to expression of doubt that the recited compounds could be useful in “cancer treatment,” *per se*, “suppressing tumor growth, [and] inhibiting growth of proliferating cells.” *Id.* The PTO stated in particular that Applicants have not disclosed any “working examples,” which the PTO defined to be those examples that draw a correlation between *in vitro* or *in vivo* assays and the claimed method.

The rejection is mooted as to cancelled claims 15 and 16. Because Applicants’ disclosure contains a wealth of enabling disclosure so as to not require undue experimentation in carrying out the invention, Applicants traverse this rejection inasmuch as it might apply to claim 14 as amended.

The claim prescribes a method of treatment of specific cancers that are known to be treatable, in whole or in part, by taxol, peloruside A, and derivatives of the latter that are encompassed by the claim. For instance, Applicants teach that “the compounds of the present invention possess microtubule-stabilizing activity similar to that of Taxol® and may therefore also be useful for inhibiting the growth of tumor cells which have become resistant to Taxol®.” Thus, at the outset, the skilled artisan would at least appreciate that the inventive compounds are at least as effective as taxol on those tumor cells for which taxol is prescribed.

Buttressing this critical teaching, and in contrast to the PTO’s assertion, Applicants disclose a great deal of *in vitro* data correlating cytotoxicity assay data and treatment of the cancers now recited in the claim. Thus, for example, Table 2 tabulates the cytotoxic effect of taxol and peluroside A on various cancer cell lines. *See* specification at paragraph 0271. Additionally, Applicants teach that peluroside analogs also exhibit similar activity against cancer cells. *See* paragraphs 0276-0278 (Example 8) and Figures 76-79.

In further contrast to the PTO’s stated ground for rejection, Applicants explicitly teach suggested dosages of the peluroside analogs for use in the claimed method. *See* paragraph 0174. Moreover, exact dosages depending upon the cancer to be treated are tied to those corresponding dosages of taxol. *Id.*

In light of these considerations, the skilled artisan<sup>3</sup> would be obliged to perform no more than routine experimentation to implement Applicants’ claimed method. In summary, the artisan would have at his or her disposal, at the very least (1) Applicants’ assay data, (2) knowledge that cancers to be treated are those for which well-known taxol is prescribed, (3) Applicants’ teaching that the recited peluroside analogs and taxol share similar functions, and (4) explicit dosage requirements.

There can be no doubt, therefore, that Applicants teach how to make and use the claimed method as prescribed by the first paragraph of section 112. Applicants respectfully request, therefore, the PTO to reconsider and withdraw this ground for rejection.

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<sup>3</sup> The PTO defined the skilled artisan to be “a physician with a MD degree and of several years of experience.” Office Action at page 6.

### CONCLUSION

Having advanced reasonable grounds for the withdrawal of each of the PTO's stated rejections and objection, Applicants believe that the present application is now in condition for allowance. Applicants therefore request Favorable reconsideration of the application as amended. Examiner Owens is courteously invited to contact the undersigned by telephone if she feels that any remaining issues warrant a discussion.

Respectfully submitted,

Date May 18, 2007

By 

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**The Commissioner is hereby authorized to charge any additional fees, which may be required regarding this application under 37 CFR §§ 1.16-1.17, and to credit any overpayment to Deposit Account No. 19-0741. Should no proper payment accompany this response, then the Commissioner is authorized to charge the unpaid amount to the same deposit account. If any extensions of time are needed for timely acceptance of submitted papers, then Applicants petition for such extension under 37 CFR §1.136 and authorize payment of any such extensions fees to the deposit account.**